REMARKS

Claims 8 and 10 have been cancelled, without prejudice.

Claim 1 has been amended to recite "[a]n isolated modified mevalonate kinase which exhibits a sensitivity to feedback inhibition which is reduced in comparison to the corresponding non-modified mevalonate kinase wherein

the modified mevalonate kinase contains a mutation when compared with the amino acid sequence of the corresponding non-modified mevalonate kinase wherein the mutation is at the amino acid position corresponding to amino acid position 17 of the sequence as shown in SEQ ID NO:1, and

wherein the modified mevalonate kinase is at least 95% homologous to SEQ ID NO:1." Support for this amendment is found in the specification at, for example, page 3, lines 9-15; page 7, lines 9-15; in Examples 1-10; and in original claims 1 and 8. *See In re Gardner*, 177 USPQ 396, 397 (CCPA 1973) and MPEP §§ 608.01(o) and (l) (8th ed. Rev. 6, Sept. 2007, pp. 600-92 and 600-84).

Claim 19 has been amended to recite "[a] method for producing the modified mevalonate kinase according to claim 1 comprising:

(a) culturing in a suitable medium a population of host cells, which comprise a vector or plasmid that comprises a polynucleotide that encodes the modified mevalonate kinase wherein

the modified mevalonate kinase contains a mutation when compared with the amino acid sequence of the corresponding non-modified mevalonate kinase wherein the mutation is at the amino acid position corresponding to amino acid

position 17 of the sequence as shown in SEQ ID NO:1 and the modified mevalonate kinase is at least 95% homologous to SEQ ID NO:1; and

(b) optionally recovering the modified mevalonate kinase from the cells or from the medium." Support for this amendment is found in the specification at, for example, page 3, lines 9-15; page 7, lines 9-15; in Examples 1-10; and in original claims 1 and 8. (*Id.*).

Claim 20 has been amended to recite "[a] method for the preparation of a mevalonate kinase having reduced sensitivity to feedback inhibition, comprising the following steps:

(a) providing a polynucleotide encoding a first mevalonate kinase which exhibits sensitivity to feedback inhibition;

(b) introducing a mutation into the polynucleotide sequence such that the mutated polynucleotide sequence encodes a second mevalonate kinase which contains a mutation when compared to the first mevalonate kinase wherein the mutation is at the amino acid position corresponding to amino acid position 17 of the sequence as shown in SEQ ID NO:1, and

wherein the second mevalonate kinase is at least 95% homologous to SEQ ID NO:1;

(c) optionally inserting the mutated polynucleotide in a vector or plasmid;

(d) introducing the mutated polynucleotide or the vector or plasmid into a suitable host cell; and

(e) culturing the host cell under conditions that allow expression of the second mevalonate kinase." Support for this amendment is found in the specification at, for example, page 3, lines 9-15; page 7, lines 9-15; in Examples 1-10; and in original claims 1 and 8. (*Id.*).

Claims 2-4 and 9 have been amended to recite "[t]he modified mevalonate kinase according to ...." These amendments have been made for clarification purposes only and do not change the scope of the claims in anyway.

Claim 11 has been amended to recite "the modified mevalonate kinase according to ...." Claim 12 has been amended to recite "[t]he polynucleotide according to ...." Claim 13 has been amended to recite "[a] vector or plasmid comprising the polynucleotide according to ...." Claim 14 has been amended to recite "[t]he vector or plasmid according to ...." Claim 16 has been amended to recite "[t]he host cell according to ...." These amendments have been made for clarification purposes only and do not change the scope of the claims in anyway.

Claim 16 has been further amended to include proper Markush language. This amendment has been made for clarification purposes only and does not change the scope of the claim in any way.

The specification at page 19, lines 1-8, first paragraph, has been amended to recite sequence identifiers for all the sequences that appear in drawing Figure 1.

It is submitted that no new matter has been introduced by the foregoing amendments. Approval and entry of the amendments is respectfully solicited.

INTERVIEW SUMMARY

The Examiner is thanked for the courtesies extended during a telephonic Interview conducted with the undersigned on November 26, 2007 ("Examiner's Inteview"). During the Examiner's Interview, the foregoing amendments, the pending objections, and the pending rejections under 35 U.S.C. §§ 101 and 112 were discussed. The Examiner agreed that the amendments presented above would likely place the application in condition for allowance. Therefore, in view of the amendments and remarks below, withdrawal of the objections and rejections, and allowance of the claims are respectfully requested.

Objections:

1. Drawing Objection

The Examiner objected to "[t]he drawings ... for disclosing sequences that are not identified by a sequence identifier number (SEQ ID NO:)." (Paper No. 20071010 at 2).

Initially, we note that Figure 1 is the only drawing figure to disclose sequences. Figure 1 shows a multiple amino acid sequence alignment for different mevalonate kinases. Each sequence in Figure 1 was part of the Sequence Listing as originally filed. With a view towards furthering prosecution, the brief description of the drawings for drawing Figure 1 at page 19, lines 1-8, first paragraph, has been amended to recite sequence identifiers for all the sequences that appear in the drawing figure. As discussed in MPEP §§ 2429 and 2422.02, nothing more is required.

See MPEP § 2429 (8th ed. Rev. 6, Sept. 2007, p. 2400-55) ("Figures can be used to convey information not readily conveyed by the Sequence Listing. ***The exclusive conformance requirement of 37 CFR 1.821(b) will be relaxed for drawing figures.*** However, the sequence information so conveyed must still be included in a 'Sequence Listing' and the sequence identifier ('SEQ ID NO:X') must be used, either in the drawing or in the 'Brief Description of the Drawings.'") (emphasis added); *see also* MPEP § 2422.02 (8th ed. Rev. 6, Sept. 2007, pp. 2400-33 and 2400-34) ("In view of the fact that many significant sequence characteristics may only be demonstrated by a figure, the exclusive conformance requirement of this section may be relaxed for drawing figures." "***Further, the similarity or homology between/among sequences can only be depicted in an effective manner in a***

drawing figure. Similarly, drawing figures are recommended for use with amino acid sequences to depict structural features of the corresponding protein, such as finger regions and Kringle regions. The situations discussed herein are given by way of example only and there may be many other reasons for relaxing the requirements of this section for the drawing figures. It should be noted, though, that when a sequence is presented in a drawing, regardless of the format or the manner of presentation of that sequence in the drawing, the sequence must still be included in the Sequence Listing and the sequence identifier ('SEQ ID NO:X') must be used, either in the drawing or in the Brief Description of the Drawings.") (emphasis added).

In view of the foregoing, the drawing objection is rendered moot. Accordingly, withdrawal of the drawing objection is respectfully requested.

2. Claim Objections

The Examiner objected to claims 1-4, 8-16, and 19-20 "for reciting non-elected subject matter." (Paper No. 20071010 at 3).

With a view towards furthering prosecution, claims 8 and 10 have been cancelled, without prejudice, and claims 1-4, 9, 11-16, and 19-20 have been amended to recite only elected subject matter. In view of the foregoing amendments, the objection of the claims is rendered moot. Accordingly, withdrawal of the objection is respectfully requested.

Rejection under 35 U.S.C. § 101:

Claims 1-4 and 8-16 were rejected under 35 U.S.C. § 101. (Paper No. 20071010 at 3). In making the rejection, the Examiner asserted that "the claimed invention is directed to non-statutory subject matter." (*Id.*). The Examiner further

asserted that "[t]he modified mevalonate kinases of [c]laims 1-4 and 8-10, the polynucleotides of [c]laims 11-14, and the host cells of [c]laims 14-16 are likely to occur in nature and, therefore, the recited products do not show the 'hand of man.'" (*Id.*).

With a view towards furthering prosecution, claims 8 and 10 have been cancelled, without prejudice, and claim 1 (from which claims 2-4, 9, and 11-16 either directly or indirectly depend) has been amended to recite "[a]n isolated modified mevalonate kinase." In view of the foregoing amendments, the rejection of claims 1-4, 9, and 11-16 under 35 U.S.C. § 101 is rendered moot. Accordingly, withdrawal of the rejection is respectfully requested.

Indefiniteness Rejections:

Claims 2-4, 8-16, 19, and 20 were rejected under 35 U.S.C. § 112, second paragraph. (*Id.*). In making this rejection, the Examiner asserted that "[f]or [c]laims 2-4, 8-12, and 19, the phrase 'A [a] modified mevalonate kinase according to claim ...' should be corrected to 'The [the] modified mevalonate kinase according to claim ....'" (*Id.*). The Examiner further asserted that "[f]or [c]laims 12 and 13, the phrase 'A [a] polynucleotide according to claim 11' should be corrected to 'The [the] polynucleotide according to claim 11.'" (*Id.*). The Examiner further asserted that "[f]or [c]laim 14, 'A vector or plasmid according to claim 13' should be corrected to 'The vector or plasmid according to claim 13.'" (*Id.*). The Examiner further asserted that "[f]or [c]laim 16, 'A host cell according to claim 15' should be corrected to 'The host cell according to claim 15.'" (*Id.*). The Examiner finally asserted that "[f]or [c]laim 20(d), the phrase 'the polynucleotide' renders the claim indefinite" because "[i]t is unclear whether

said phrase refers to the polynucleotide encoding the first or second mevalonate kinase." (*Id.*).

With a view towards furthering prosecution, claims 8 and 10 have been cancelled, without prejudice, and, as suggested by the Examiner, claims 2-4, 9, 11, 12, and 19 have been amended to recite "[t]he modified mevalonate kinase according to ...." As suggested by the Examiner, claims 12 and 13 have been amended to recite "[t]he polynucleotide according to ...." As also suggested by the Examiner, claim 14 has been amended to recite "[t]he vector or plasmid according to ...." As also suggested by the Examiner, claim 16 has been amended to recite, *inter alia*, "[t]he host cell according to ...." Also, claim 20 has been amended to recite "the mutated polynucleotide." In view of the foregoing amendments, the rejections of claims 2-4, 9, 11-16, 19, and 20 are rendered moot. Accordingly, withdrawal of the rejections is respectfully requested.

§112, First Paragraph Rejections:

1. Enablement

Claims 1-4, 8-11, 13-16, 19, and 20 have been rejected under 35 U.S.C. §112, first paragraph, for lack of enablement. (Paper No. 20071010 at 4). In making the rejection, the Examiner acknowledged that the specification is "enabling for the polypeptide of SEQ ID NO: 1 having an $Ile^{17}Thr$ substitution, ..." (*Id.*).

The Examiner, however, asserted that the specification "does not reasonably provide enablement for any variant of SEQ ID NO: 1, having any structure comprising a substitution at Ile^{17}, and having melavonate kinase activity with decreased feedback sensitivity." (*Id.*).

As is well settled, it is the Examiner's burden to demonstrate that a specification is not sufficiently enabling. *In re Marzocchi*, 169 USPQ 367, 369 (CCPA 1971). To carry this burden, the Examiner must identify and clearly articulate the factual bases and supporting evidence that allegedly establish that undue experimentation would be required to carry out the claimed invention. *Id.* at 370.

With a view towards furthering prosecution, and as agreed during the Examiner's Interview, independent claim 1 (from which claims 2-4, 9, 11-16, and 19 either directly or indirectly depend) has been amended to recite "[a]n isolated modified mevalonate kinase which exhibits a sensitivity to feedback inhibition which is reduced in comparison to the corresponding non-modified mevalonate kinase wherein

the modified mevalonate kinase contains a mutation when compared with the amino acid sequence of the corresponding non-modified mevalonate kinase wherein the mutation is at the amino acid position corresponding to amino acid position 17 of the sequence as shown in SEQ ID NO:1, and

wherein the modified mevalonate kinase is at least 95% homologous to SEQ ID NO:1." And, independent claim 20 has been amended to recite "[a] method for the preparation of a mevalonate kinase having reduced sensitivity to feedback inhibition, comprising the following steps:

(a) providing a polynucleotide encoding a first mevalonate kinase which exhibits sensitivity to feedback inhibition;

(b) introducing a mutation into the polynucleotide sequence such that the mutated polynucleotide sequence encodes a second mevalonate kinase which contains a mutation when compared to the first mevalonate kinase wherein the

mutation is at the amino acid position corresponding to amino acid position 17 of the sequence as shown in SEQ ID NO:1, and

wherein the second mevalonate kinase is at least 95% homologous to SEQ ID NO:1;

(c) optionally inserting the mutated polynucleotide in a vector or plasmid;

(d) introducing the mutated polynucleotide or the vector or plasmid into a suitable host cell; and

(e) culturing the host cell under conditions that allow expression of the second mevalonate kinase."

In view of the foregoing amendments and the agreement reached during the Examiner's Interview, it is respectfully submitted that the rejection has been rendered moot and should be withdrawn.

2. Written Description

Claims 1-4, 8-11, 13-16, 19, and 20 have been rejected under 35 U.S.C. §112, first paragraph, for lack of written description. (Paper No. 20071010 at 7). In making the rejection, the Examiner asserted that claims 1-4, 8-11, 13-16, 19, and 20 "contain[] subject matter, which was not described in specification ...." (*Id.*). The Examiner also asserted that the claims "are directed to a genus of polypeptides comprising all variants of SEQ ID NO: 1, having any structure comprising a substitution at Ile^{17}, and having melavonate kinase activity with decreased feedback sensitivity." (*Id.*). The Examiner further asserted that "[t]he specification teaches the structure of only a single representative species of such polypeptides." (*Id.*). The Examiner then

concluded that "[g]iven this lack of description of representative species encompassed by the genus of the claim, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicants were in possession of the claimed invention." (*Id.*).

With a view towards furthering prosecution, and as agreed during the Examiner's Interview, independent claims 1 and 20 have been amended as described above.

In view of the foregoing amendments and the agreement reached during the Examiner's Interview, it is respectfully submitted that the rejection has been rendered moot and should be withdrawn.

Accordingly, for the reasons set forth above, entry of the amendments, withdrawal of the objections and rejections, and allowance of the claims are respectfully requested. If the Examiner has any questions regarding this paper, please contact the undersigned.

I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as first class mail in an envelope addressed to: Mail Stop Amendment, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on January 2, 2008.

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Respectfully submitted,

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